UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,956	04/27/2005	Jakob Busch-Petersen	P51376	9137

20462 7590 11/06/2006

SMITHKLINE BEECHAM CORPORATION
CORPORATE INTELLECTUAL PROPERTY-US, UW2220
P. O. BOX 1539
KING OF PRUSSIA, PA 19406-0939

EXAMINER	
BERNHARDT, EMILY B	
ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 11/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/532,956	BUSCH-PETERSEN ET AL.	
	Examiner	Art Unit	
	Emily Bernhardt	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/27/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The abstract of the disclosure is objected to because the structural formula corresponding to applicants' invention should be shown. Correction is required. See MPEP § 608.01(b).

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is of indeterminate scope for the following reason. Defining a disease(s) by its (their) underlying cause renders the scope of intended uses indeterminate since the claim language may read on diseases not yet known to be caused by or affected by such action or in ways not yet understood. Additionally, determining whether a given disease responds or not to such a mode of action (i.e. binding to IL-8 receptors) involves much experimentation since a negative response from one patient does not mean the drug isnt useful as no drug has 100% effectiveness. Thus what " success rate" determines if a particular inhibitor is effective and how many patients (and dosage regimens) need to be tested? The test for determining compliance with 35 USC 112, par.two is whether applicants have clearly defined "their invention" not what may be discovered by future research as this type of claim language clearly requires.

Claims 3 and 4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Scope of diseases covered by claims 3 and 4 are not remotely enabled based solely on instant compounds' ability to selectively antagonize IL-8 receptors in *in vitro* assays described in the specification . No clear evaluation of their relevance to *in vivo* efficacy for any one use is ever set forth much less to all the myriad of uses claimed which include treating skin, pulmonary disorders, all viruses as well as Alzheimer's Disease, malaria, stroke, ulcerative colitis and many more. The references cited in the specification do not indicate that there are any known IL-8 anatgonists for any one use much less the scope provided. See also Matsukawa, a more recent publication, which stresses for just inflammation, that *in vitro* studies do not clearly establish a definitive role in vivo . Also see Melter for organ transplantation who discusses the likelihood of many types of chemokines being implicated but concludes that much more *in vivo* studies in animals and man are needed to determine efficacy. The examiner could not find any references even linking IL-8 to the treatment of Alzheimer's or malaria ..

Where the utility is unusual or difficult to treat or speculative, the examiner has authority to require evidence that tests relied on are reasonably predictive of in vivo efficacy by those skilled in the art. See for example, In re Ruskin 148 USPQ 221; Ex parte Jovanovics 211 USPQ 907. Note MPEP. 2164.05(a). Any evidence relied on by applicants must clearly show a reasonable expectation of *in vivo* success for any additional diseases that may still be embraced in response to this action. See MPEP. 2164.05(a). Note also the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a),August 2000 edition which considers factors such as:

1) Breadth of the claims- The claims cover (but are not limited to) to all types of skin, pulmonary and inflammatory diseases, as well as Alzheimer's disease, gastrointestinal disorders, viruses,sepsis as well as diseases that may be covered by aberrant angiogenesis, restenosis and many others ;

2) Level of skill in this art- as far as the examiner is aware there are no known drugs in clinical trials having the activity relied on herein much less known for such a spectrum of clinical applications. Note concluding remarks in Li on p.1909, right column and thus the level of skill is low. ;

3) State of the prior art- compounds similar in structure have not been reported to be clinically active for such a range of uses;

4) Direction or Guidance- the dosage range information (on p.22-23) is

virtually useless being much greater than 100-fold range and not directed to a specific disease;

5) Working examples- There are no test(s) directed to the many uses pointed out above which are art-recognized for predicting *in vivo* efficacy .

Thus in view of the above the rejection is being applied.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jin (WO'442). The commonly assigned publication which published more than a year earlier of applicants' US priority date describes similar compounds having the same mechanism of action from which various uses are asserted which includes those claimed herein. See pages 1-4 and in particular piperazino species on p.10, lines 20-21. Said species differ only in the presence of 2 chlorines on phenyl ring in place of instant 2-chloro-3-fluorophenyl derivatives in claims 1-4. Note that Jin teaches all halos as suitable substituents on the phenyl ring as can be seen from the definition of

"Y" on page 4. Thus it would have been obvious to one skilled in the art at the time the instant invention was made to replace either chloro with fluorine and in so doing obtain a compound within the instant scope for intended uses described by Jin.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is 571-272-0664.

If attempts to reach the examiner by telephone are unsuccessful, the acting supervisor for AU 1624, James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

E Bernhardt

Emily Bernhardt
Primary Examiner
Art Unit 1624